Uterine Vascular Lesions

Abhishek Vijayakumar, MS,[1] Amruthashree Srinivas, MD,[2] Babitha Moogali Chandrashekar, MD,[3] Avinash Vijayakumar, MD[4]

[1]Department of General Surgery, Victoria Hospital, Bangalore Medical College and Research Institute, Bangalore, India; [2]Department of Obstetrics and Gynecology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [3]Department of Obstetrics and Gynecology, Mysore Medical College and Research Institute, Mysore, India; [4]Department of Radiology, Banaras Hindu University, Uttar Pradesh, India

Vascular lesions of the uterus are rare; most reported in the literature are arteriovenous malformations (AVMs). Uterine AVMs can be congenital or acquired. In recent years, there has been an increasing number of reports of acquired vascular lesions of the uterus following pregnancy, abortion, cesarean delivery, and curettage. It can be seen from these reports that there is confusion concerning the terminology of uterine vascular lesions. There is also a lack of diagnostic criteria and management guidelines, which has led to an increased number of unnecessary invasive procedures (eg, angiography, uterine artery embolization, hysterectomy for abnormal vaginal bleeding). This article familiarizes readers with various vascular lesions of the uterus and their management.

[Rev Obstet Gynecol. *2013;6(2):69-79 doi: 10.3909/riog0207*]

KEY WORDS

Uterine arteriovenous malformations • Uterine hemangioma • Placental chorioangioma • Uterine arteriovenous fistula • Uterine pseudoaneurysm • Acquired AVM

Vascular lesions of the uterus are very rare; most reported in the literature are arteriovenous malformations (AVMs). Uterine vascular malformations can be congenital or acquired. Recently, there has been a rise in the number of reported cases following pregnancy, abortion, and curettage. Many of these studies report spontaneous resolution of vascular lesions during follow-up; in addition, there is an increasing trend toward use of uterine artery embolization (UAE) to treat these lesions. In many of the reported studies, the diagnosis of uterine vascular malformation was made as early as the second day after

a delivery or an abortion. In a study by Timmerman and colleagues,[1] out of 30 cases reported as uterine AVM based on Doppler study, only 3 were true AVMs. Rufener and associates[2] conducted a sonologic evaluation of postpartum and postabortion uterine vascular lesions that were reported as AVMs; the study revealed that, on pathologic examination, none turned out to be AVMs. Thus, we observe that there is confusion with regard to the terminology of vascular lesions such as uterine AVM, vascular malformation, arteriovenous fistula (AVF), and non-AVM vascular abnormalities of the uterus. The term *malformation*, however, is generally used to describe defects in the structure of an organ or region of the body resulting from an intrinsically abnormal process of development. Therefore, spontaneous resolution of a malformation in a short period of time is unlikely. An investigation by Mulliken and Glowacki,[3] published in 1982, provided the groundwork for a proper identification of vascular lesions. Vascular tumors grow by cellular (mainly endothelial) hyperplasia: the very common hemangioma is, in reality, a benign vascular tumor. In contrast, vascular malformations have a quiescent endothelium and are considered to be localized defects of vascular morphogenesis, likely caused by dysfunction in pathways regulating embryogenesis and vasculogenesis. Therefore, the terms *vascular abnormality* or *vascular lesion* seem to best describe hypervascular areas within the uterus seen on color Doppler ultrasound, unless they are proven to be an AVM by angiography or pathologic examination. Many of these vascular lesions are increasingly being managed by UAE. Although there have been various reports of successful pregnancy following UAE, there have also been reports of ectopic pregnancy following UAE.[4]

It is important to correctly identify various vascular lesions in the uterus to avoid unnecessary invasive intervention. This article aims to familiarize the reader with various vascular lesions of the uterus and their management.

Uterine AVM is a rare condition, and the true incidence is not yet known. A study by O'Brien and associates[5] showed an incidence of AVM of 4.5% in 464 pelvic sonographic examinations performed for pelvic bleeding. AVM has been described in patients between 18 and 72 years of age, and may be congenital or acquired pathologic conditions.[6] The congenital form is very rare and is the result of a defect in embryonic vascular differentiation or a premature arrest in the development of the capillary plexus leading to multiple abnormal connections between arteries and veins.[7] These congenital AVMs often penetrate the surrounding tissue and can cause an elaborate collateral vascular network. Furthermore, these congenital lesions can grow as pregnancy progresses.[8]

It is important to correctly identify various vascular lesions in the uterus to avoid unnecessary invasive intervention.

The International Society for the Study of Vascular Anomalies classification system divides vascular anomalies into two primary biologic categories: (1) vasoproliferative or vascular neoplasms and (2) vascular malformations. The major distinction between the two categories is whether there is increased endothelial cell turnover, which is ultimately determined by the identification of mitoses seen on histopathology. Vasoproliferative neoplasms have increased endothelial cell turnover (ie, they proliferate and undergo mitosis) because they are neoplasms. Vascular malformations do not have increased endothelial cell turnover; rather, they are structural abnormalities of the capillary, venous, lymphatic, and arterial system, and can be congenital or acquired.

Vasoproliferative Lesions of the Uterus

Uterine Hemangioma

Uterine hemangioma was first described in 1897 and was an incidental discovery from an autopsy of a young woman who developed anemia and dyspnea and died 24 hours after delivering twins. Its exact incidence still remains unclear owing to the extremely small number of case reports in the past century, with fewer than 60 cases reported to date. These lesions pass through two phases: the proliferative phase (0-12 months) and the involution phase (1-5 years). The cells lining the vascular spaces are immunoreactive for endothelial markers, including von Willebrand factor, CD31, and CD34. In contrast, the mesothelial markers, including calretinin and cytokeratin, yield negative results. These vascular markers are present in both the proliferative and involuting phases, but are lost in the fully involuted lesions.[9]

Congenital hemangioma is believed to be associated with hereditary disease, including Klippel-Trénaunay syndrome, hereditary hemorrhagic telangiectasia, tuberous sclerosis, blue rubber bleb nevus syndrome, Maffucci syndrome, and Kasabach-Merritt syndrome.[10] The endothelium is usually in the proliferative phase. Acquired hemangioma is associated with both physical changes and hormonal alterations.[11] Most of the reported cases are classified as acquired hemangioma, and the endothelia are usually in the involuting or involuted phase.

The clinical symptoms range from none (asymptomatic) to abdominal pain, excessive vaginal bleeding, anemia, infertility, and maternal and pregnancy-associated complications. Pregnant women are most commonly reported as having complications such as postpartum hemorrhage or disseminated intravascular coagulation (DIC). The hormone alterations that occur during pregnancy and the physical changes (eg, increased blood volume) of the uterine structure during pregnancy or delivery may affect preexisting lesions and thus trigger DIC. The pathophysiology of DIC is generally presumed to be platelets trapped in the abnormally proliferating endothelium within the hemangioma. Computed tomography (CT), angiography, and magnetic resonance imaging (MRI) are the various imaging modalities used in the diagnosis of these lesions; ultrasound-guided biopsy can be performed for pathologic diagnosis.[12]

Various treatment options are available, such as carbon dioxide laser excision, knife excision, cryotherapy, radiotherapy, electrocauterization, internal artery ligation, UAE, local excision, conization, and laser ablation. If hemangiomas are refractory to conservative treatments, hysterectomy may be considered.[13]

Hemangiomas associated with pregnancy are best managed with vaginal delivery. It is important to remember that vascular lesions increase in size during pregnancy and are at risk of causing postpartum hemorrhage due to the inability of thin-walled vessels to contract, in addition to rupture of congested vessels. Hypervascularity and large cross-sectional areas of vessels increase risk for amniotic fluid embolization. Care must be taken not to incise over a lesion during cesarean delivery; it is preferable to place a vertical incision.[14]

Placental Chorioangioma

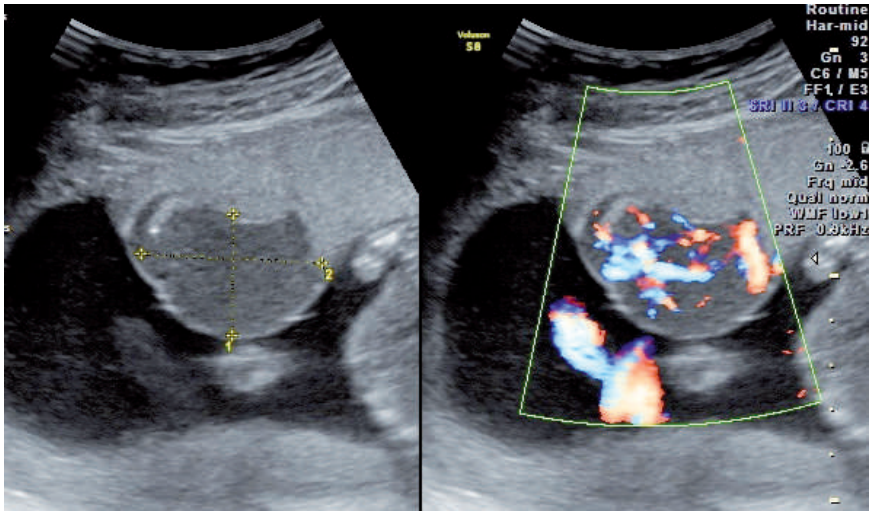
Placental chorioangioma is the most common benign tumor of the placenta. The largest retrospective study of 22,000 placental examinations showed 138 chorioangiomas with an incidence of 0.6%.[15] Chorioangioma is believed to develop by the 16th day of fertilization, although there is no documentation of tumors developing in the first trimester of pregnancy. Placental chorioangioma consists of a benign angioma arising from chorionic tissue. Marchetti[16] described three histologic patterns of chorioangiomas: angiomatous, cellular, and degenerate. The angiomatous is the most common, with numerous small areas of endothelial tissue, capillaries, and blood vessels surrounded by placental stroma. These lesions are sometimes classified as placental hamartomas rather than true neoplasia. There is no malignant potential.

Tumors $<$ 5 cm are usually asymptomatic and unlikely to cause maternal and fetal complications. Large tumors probably act as arteriovenous shunts and cause complications. Maternal complications include preeclampsia, preterm labor, placental abruption, and polyhydramnios. Fetal congestive heart failure may develop because of the increased blood flow through the low-resistance vascular channels in the chorioangioma that act as an arteriovenous shunt. Other complications include hydrops, hemolytic anemia, congenital anomalies, fetal thrombocytopenia, cardiomegaly, and growth restriction.

Gray-scale ultrasound findings show a well-defined complex echogenic mass different in appearance from the rest of the placenta; the tumor protrudes into the amniotic cavity near the umbilical cord insertion. On Doppler imaging, the feeding vessel usually has the same pulsatile flow as that of the umbilical artery but may have an arteriovenous shunt, causing low-resistance flow.[17] Chorioangiomas are isointense on T1-weighted images, with increased signal intensity on T2-weighted images. Focal areas of increased signal intensity on T1- and T2-weighted images correspond to intralesion hemorrhage. Placental teratomas are extremely rare and are similar in appearance to chorioangiomas, but are differentiated by the presence of calcifications (Figure 1).

Chorioangioma with complications before fetal viability requires

Figure 1. Sonography of placental chorioangioma. A well-defined oval hypoechoic lesion arising from the fetal surface of the placenta with significant internal vascularity on Doppler; there is no evidence of calcification.



intervention. Various techniques with varying success rates have been attempted, such as serial fetal transfusions,[18] fetoscopic laser coagulation of vessels supplying the tumor,[19] chemosclerosis with absolute alcohol,[20] and endoscopic surgical devascularization. Polyhydramnios is treated with therapeutic amniocentesis and maternal indomethacin therapy.[21]

Vascular Malformations

Venous malformation (VM) is the most common symptomatic vascular malformation. Typically, these anomalies are caused by germline or somatic mutations in the *TIE2* gene, which is involved in signaling between the endothelial and the mesenchymal cells during vasculogenesis and angiogenesis.[22] These anomalous veins have endothelial cellular abnormalities and severe deficiency of the smooth muscle layer, resulting in gradual stretching and expansion of the lumen over time. The malformed veins become distended with dependency or increased venous pressure.[22]

VMs of the uterus and ovaries are typically associated with insufficiency of the ovarian vein and probably form a subtype of "pelvic congestion syndrome." Patients with extensive VMs may develop localized intralesional coagulopathy resulting in a systemic DIC, especially in association with surgery (Figure 2).

VMs are readily diagnosed by MRI. These lesions are highly hyperintense on T2-weighted images, often contain thrombi or phleboliths, and enhance inhomogeneously. Treatment is by endovascular ablation using either absolute ethanol or 3% sodium tetradecyl foam[23] or surgical excision; some patients who are at increased risk for thromboembolism have to be maintained on lifelong anticoagulation.

Arteriovenous Fistula

Although uterine AVF is uncommon, it can be the cause of irregular uterine bleeding, and can also provoke massive life-threatening uterine hemorrhage. Uterine AVF has been reported to occur as a consequence of previous uterine trauma such as prior pelvic surgery and curettage[24]; there have also been reports of placental site trophoblastic tumors presenting as AVF.[25] It normally represents a single connection between an artery and a vein without being supplied by extrauterine arteries or having a nidus. The most common AVFs are aortocaval fistulae, followed by ilioiliac and aortoiliac fistulae.[26] The basic architecture of an AVF is that of a low-pressure sump. Eight cases of uterine vessel AVFs following hysterectomy have been reported, most recently in 1990.[27,28]

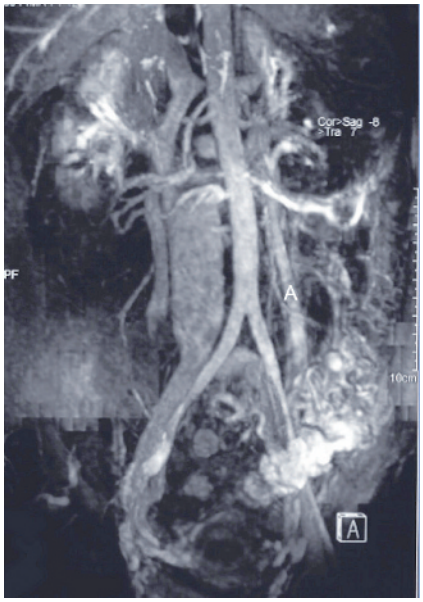


Figure 2. Magnetic resonance imaging signs of pelvic reflux from venous malformation. The maximum-intensity projection image demonstrates dilated parauterine varices filled due to passive reflux of contrast.

Acquired AVFs, secondary to surgery or trauma, tend to occur in younger patients because trauma or surgery tends to affect younger patients. In contrast, spontaneous perforation of atherosclerotic aneurysm into adjacent veins tends to occur in the older population.

Although the exact etiology is unknown, it is known that both the cardinal ligaments (composed of a network of multiple tortuous arteries and veins) and the uterine artery and vein are routinely ligated and transected en bloc during hysterectomy. The application of transfixation sutures to the ligature may inadvertently create a connection between an artery and vein. Fistulae might form in cases in which the wound was packed or clamps were left in place after wound closure because of uncontrolled bleeding; this could indicate inadequate ligation of the vessels. Blood is shunted from the high-pressure arterial side to the low-pressure venous side following bilateral transfixion ligatures in the uterine vessel portion of the cardinal ligament. This creates an abnormal low-resistance circuit that steals from the high-resistance normal capillary bed.[29,30]

This connection will classically enlarge over time: first, with hypertrophy of the feeding vessel, and then with hypertrophy of the draining vessel. This may lead to a decreased arterial blood supply to the distal limb. Clinical awareness of this potential postoperative complication is important, as AVF can lead to catastrophic bleeding. On clinical examination patients may have a pulsatile pelvic mass or abnormal vascularity in the lower genital track. Throbbing pelvic, vaginal, rectal, or leg pain, menorrhagia, and dyspareunia are the major presenting symptoms reported. High-output cardiac failure is reported in nearly 20% of cases (Figure 3).[31]

Although uterine AVF is uncommon, it can be the cause of irregular uterine bleeding, and can also provoke massive life-threatening uterine hemorrhage.

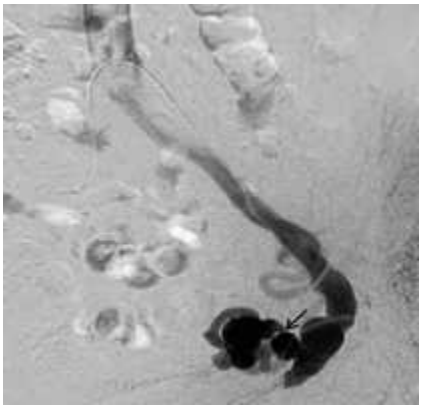


Figure 3. A pelvic angiogram demonstrating a well-visualized arteriovenous fistula (*arrow*) with the catheter in the artery and early filling veins; note the absence of nidus.

Imaging modalities used in diagnosis are Doppler ultrasound, CT angiography, and magnetic resonance angiography, which have better delineation of soft tissues. Treatment is relatively easy due to single communication between artery and vein. The therapy is aimed at complete closure of the fistula with an endovascular or open surgical procedure. The principal endovascular options are coil embolization and stent grafting. Metallic coils are preferred because of the risk of shunting particulate embolic materials via a fistula into the systemic circulation.[32] Choosing a coil size slightly larger than the vessel is the most important part of the procedure, to avoid passage through the AVF. However, where access is difficult or the procedure carries a high risk for complications, a venous covered stent may be used.[33]

Pseudoaneurysm

A pseudoaneurysm is an extraluminal collection of blood with turbulent flow that communicates with the parent vessel through a defect in the arterial wall. The development of an arterial pseudoaneurysm is a rare but reported complication of pelvic surgery,[34] vascular trauma during cesarean delivery,[35] or after uterine curettage. Under the influence of sustained arterial pressure, blood dissects into the tissues around the damaged artery and forms a perfused sac that communicates with the arterial lumen. The absence of a three-layer arterial wall lining the pseudoaneurysm differentiates it from a true aneurysm, which is less common.

Pseudoaneurysm of the uterine artery is an uncommon cause of delayed postpartum hemorrhage following caesarean or vaginal delivery and is potentially life threatening. Typically, the lesions are discovered because the patients have symptoms related to delayed rupture of the pseudoaneurysm, causing hemorrhage.[36] A pseudoaneurysm may be asymptomatic, may thrombose, or may lead to distal painful embolization. The risk for rupture is proportional to the size and intramural pressure.

Pseudoaneurysm of the uterine artery is an uncommon cause of delayed postpartum hemorrhage following caesarean or vaginal delivery and is potentially life threatening.

Diagnosis is made with Doppler ultrasound, which shows swirling arterial flow; different directions and velocities are seen, with varying colors according to the degree of turbulence within the pseudoaneurysm. In the neck of the pseudoaneurysm, the "to-and-fro" pattern may be potentially identified with duplex ultrasonography because arterial blood flows like a jet (forward flow) into the aneurysm cavity during systole, then reverses (backward flow) into the original artery during diastole.[37] This pattern is explained by the pressure gradient between a distended, high-pressure pseudoaneurysm and a low-pressure artery during diastole.[38] However, in the case of a uterine artery pseudoaneurysm, demonstration of the neck of the pseudoaneurysm on ultrasound may be difficult because of the small size of the parent artery.[39] Angiography can clearly demonstrate one or more pseudoaneurysms supplied by one or more feeding arteries (Figure 4).

Treatment is immediate UAE; although surgical repair can be attempted it is rarely performed due to increased bleeding

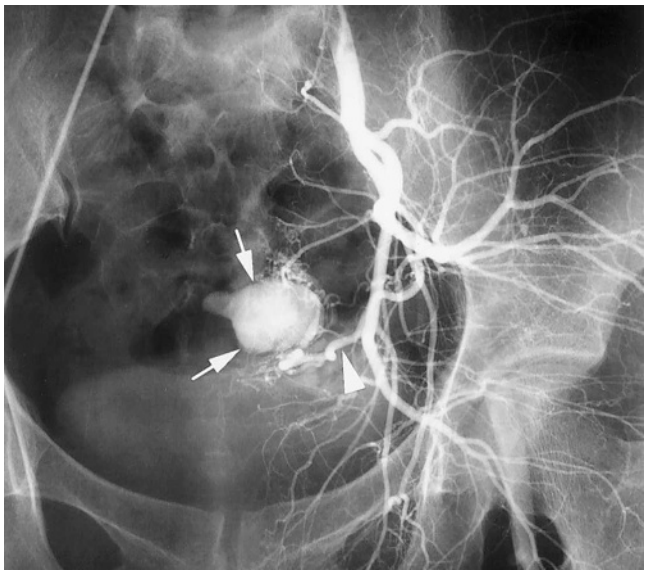


Figure 4. Pelvic angiogram showing pseudoaneurysm of the left uterine artery. The *arrows* indicate pseudoaneurysm with filling of contrast eccentrically. The *arrowhead* indicates the left uterine artery arising from the internal iliac artery.

complications. When retained villi are abundantly present within a pseudoaneurysm, rapid recruitment of collateral vessels following arterial embolization may occur from pelvic arteries, recanalizing the pseudoaneurysm.[40] Therefore, particular attention to the results of a serum β-human chorionic gonadotropin (hGC) test should be stressed. In this situation, methotrexate therapy or a retrial of uterine curettage immediately after embolization may decrease recanalization of the pseudoaneurysm. Another cause of embolization failure is inadequate embolization of a pseudoaneurysm supplied by extrauterine feeding arteries, such as the internal pudendal artery, ovarian artery, inferior epigastric artery, or contralateral uterine artery.[41] A meticulous search for other feeding arteries is recommended, including detection of simultaneous cross-filling of the sac by two or more arteries.

Arteriovenous Malformation

Congenital AVM. Although most AVMs are sporadic, several mutations have been identified. These include *ALK1* and endoglin in hereditary hemorrhagic telangiectasia, *RASA1* in familial capillary malformation AVM, and phosphatase and tensin (*PTEN*) in patients with Bannayan-Riley-Ruvalcaba syndrome or Cowden syndrome.[42,43] Uterine AVM can also be seen in hereditary hemorrhagic telangiectasia.[44]

Congenital uterine AVMs arise from an abnormality in the embryologic development of primitive vascular structures, and tend to have multiple feeding arteries and draining veins and an intervening nidus. Histologic examination of these malformations usually reveals a localized proliferation of both arterial and venous vessels with interconnecting fistulae. There are many thin-walled capillary-type vessels intertwining these muscular vessels. It has also been recognized that the proportions of different vessel types may vary.[45]

Congenital uterine AVMs arise from an abnormality in the embryologic development of primitive vascular structures…

In many cases, distinction between artery and vein becomes blurred due to secondary intimal thickening in the veins as a result of increased intraluminal pressure.

Although these vascular anomalies have been reported in both adolescence and following menopause, they tend to occur predominantly in women of reproductive age and very rarely in women who have not been pregnant. Pregnancy appears to play an important role in the pathogenesis of uterine AVMs. The pattern of bleeding is intermittent and torrential, suggestive of arterial hemorrhage. Uterine bleeding is thought to occur when vessels of the AVM are exposed from sloughing of the endometrium iatrogenically during dilation and curettage (D&C) or during menses. Color and duplex Doppler ultrasound are good screening and diagnostic tools. As mentioned previously, color Doppler ultrasonography shows multiple tortuous vessels with multidirectional flow and apparent flow reversals of juxtaposed reds and blues with different flow velocities giving a mosaic pattern. Duplex Doppler ultrasonography shows the classic features of arteriovenous shunting, which manifests as fast arterial flow with low resistance: high peak systolic velocity (PSV), an arterial spectral waveform with a high diastolic component, and a pulsatile high-velocity venous waveform with little variation in systolic-diastolic velocities. Angiography is the traditional diagnostic tool. The classic angiographic features consist of a complex tangle of vessels supplied by enlarged feeding arteries, in association with early venous drainage during the arterial phase and stasis of contrast medium within the abnormal vasculature.

Acquired AVM. AVMs are characterized by multiple unions of varying sizes between arteries and veins in the same vicinity, whereas an AFV is an abnormal direct passage between an artery and an adjoining vein.[46] Acquired uterine AVMs are usually traumatic, resulting from prior D&C, therapeutic abortion, uterine surgery, or direct uterine trauma. Less commonly, diethylstilbestrol exposure,[47] endometrial carcinoma, cervical carcinoma, and gestational trophoblastic disease have been implicated as causes of acquired uterine AVMs.

Acquired uterine AVMs are usually traumatic, resulting from prior D&C, therapeutic abortion, uterine surgery, or direct uterine trauma.

Affected patients commonly present with menorrhagia or menometrorrhagia after a miscarriage, uterine surgery, or curettage. In 30% of cases a blood transfusion is necessary.[48] Symptoms can appear very slowly or suddenly. Uchide and colleagues[49] described early postpartum bleeding as a consequence of AVM. Other symptoms are lower abdominal pain, dyspareunia and anemia secondary to blood loss. In very severe AVMs, shunting can cause cardiovascular repercussions, provoking symptoms of

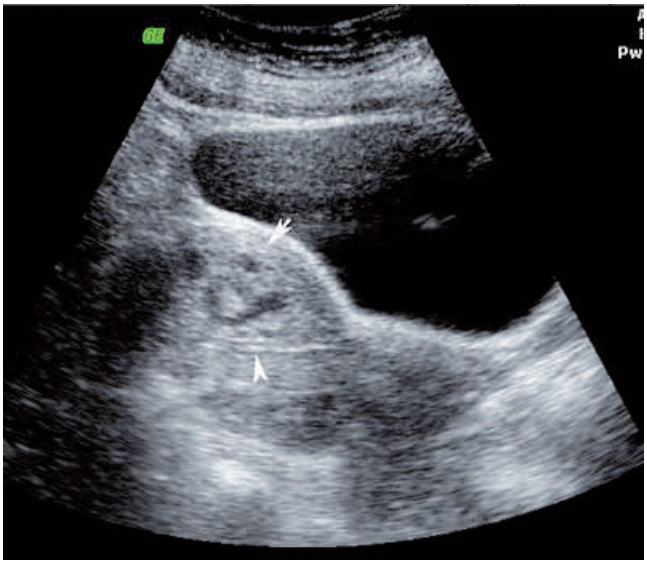


Figure 5. Gray-scale transabdominal longitudinal ultrasound image of a uterus showing multiple anechoic areas within the myometrium of the anterior wall (*arrow*) displacing the thin, linear endometrium (*arrowhead*).

dyspnea, fatigue, and even heart decompensation.

The ultrasonographic characteristics are nonspecific and include the presence of hypoechogenic tubular structures within the myometrium. Color Doppler has emerged as a screening and follow-up tool; AVMs are diagnosed on the basis of pulsatility index (PI), resistance index, PSV, and time-averaged maximum velocity. Timmerman and colleagues[1] showed that PSV could differentiate between safe and potentially dangerous AVMs. Vascular malformations with a PSV value of $\geq$ 0.83 m/s were labeled as potentially dangerous. Conversely, PSV values $<$ 0.83 m/s were labeled less dangerous vascular malformations, and PSV values $<$ 0.39 m/s were identified as safe. AVMs with high PSV were referred for immediate embolization. Postembolization PSV could predict which patients would require repeat embolization to completely cure AVM (Figure 5 and Figure 6).

Three-dimensional (3D) power color angiography, which is based on encoding the power in the Doppler signal rather than its mean frequency shift, is now emerging as a better investigative tool than color Doppler. Power Doppler equipment requires an upgrade to the software of the original color Doppler device, and thus does not require a major financial investment in new equipment. The total flow within a confined area or in a continuous vessel is displayed, giving an image similar to that of angiography. The advantage of 3D reconstruction with color power angiography images is that it demonstrates the spatial relationships of vessels more quickly (within 1 min) and easily, especially where complex structures are present. Therefore, unlike MRI, digital subtraction angiography, or contrast-enhanced CT, 3D color power angiography allows the physician to examine vascular anatomy immediately and without radiation exposure or invasive angiogram. Thus, 3D power color angiography can be used in patients with uterine lesions to confirm AVMs[50] without subjecting patients with dangerous AVM to invasive angiography and UAE (Figure 7).[51]

Angiography is the gold standard technique for diagnosing AVMs. On angiography true AVMs are recognized by early venous filling with the contrast of a vascular plexus in the endometrium or myometrium. Angiography is now reserved for those cases in which surgical intervention or therapeutic embolization is required. CT scan with contrast, nuclear MRI,[52] and hysteroscopy[53] have also been used to diagnose AVM (Figure 8).

There has been a rise in the number of reports of AVMs following pregnancy and abortion. Some points needs to be kept in mind when diagnosing post-abortion AVMs. In normal pregnancy, due to vasodilatation and decreasing resistance in the spiral arteries, a hypervascular appearance with turbulent flow (that is also referred to as *peritrophoblastic flow*) is observed, especially in the myometrium where implantation has occurred.[54] This appearance in the myometrium can also be observed in very early intrauterine gestation, even before a gestational sac visible

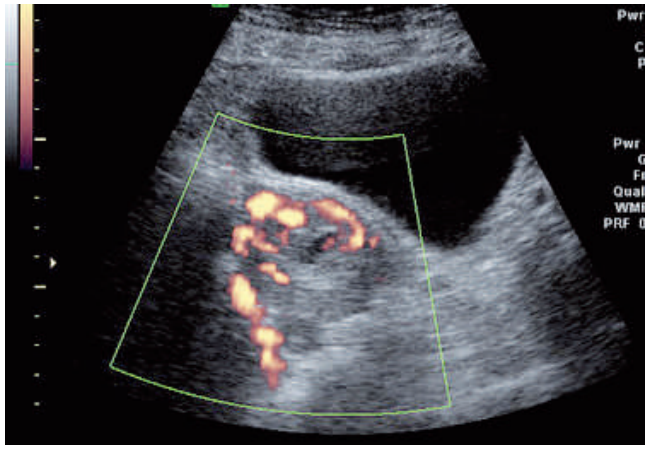


Figure 6. Power Doppler image depicting the color flow within the uterine arteriovenous malformation.

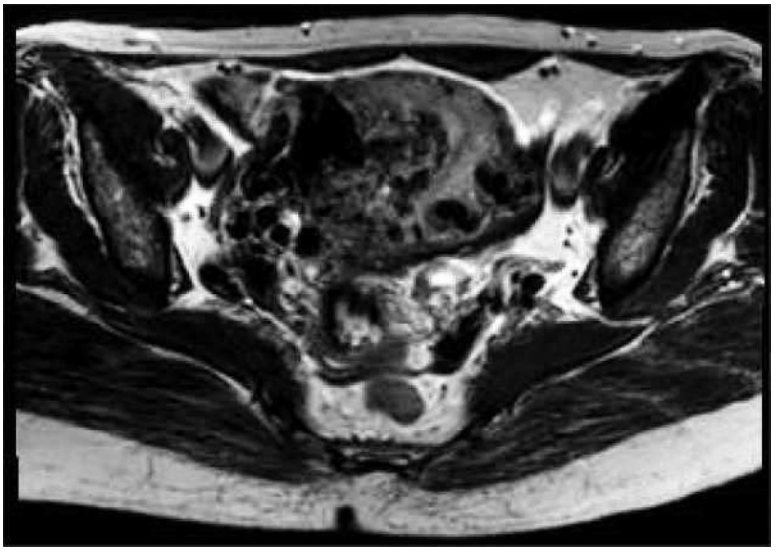


Figure 7. T2-weighted magnetic resonance image depicting a uterine arteriovenous malformation with extensive areas of signal void in the myometrium and serosal layer.

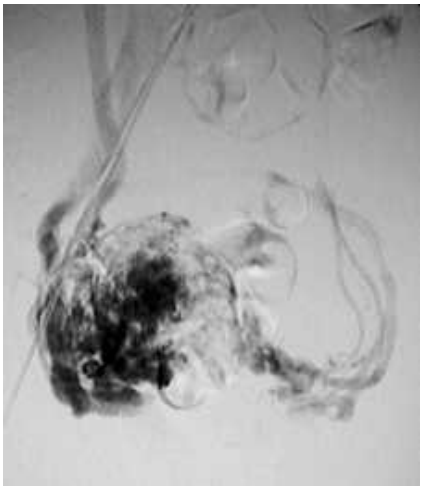


Figure 8. Pelvic angiogram showing uterine arteriovenous malformation with nidus formation.

on ultrasound appears, or following a recent spontaneous or induced abortion with an empty uterus. The hypervascularity and turbulence within the myometrium during gestation does not immediately disappear following spontaneous or induced abortion.[55] The hypervascularity gradually regresses and then disappears within the following days. This regression period is further prolonged in the presence of retained products of conception or molar gestation.[56]

In a report by Timmerman and colleagues,[1] which is the largest case series of uterine AVM in the literature, 12 of 30 patients had retained products of pregnancy at the time of diagnosis, which was pathologically confirmed to be trophoblastic tissue in six cases and molar tissue in the other six. In a study by Wiebe and Switzer,[57] a uterine AVM was diagnosed based on gray-scale and color Doppler findings in seven patients who had prolonged bleeding after an induced abortion and who were managed expectantly with the monitoring of weekly serum hCG levels. Interestingly, serum hCG was elevated in all cases, which obviously demonstrated the presence of retained trophoblastic tissue within the uterus. When hCG levels returned to normal limits, all uterine lesions disappeared spontaneously.

Retained products of conception can lead to a hypervascular appearance with turbulent flow on color Doppler imaging, not only in the endometrial cavity but also within the myometrium or in the subendometrial region. The presence of trophoblastic tissue in the myometrium or subendometrial region could be explained by the encroachment of placental tissue into these regions through damaged endometrium due to curettage. It has been recently suggested that curettage should not be performed in a patient who presents with abnormal uterine bleeding after an abortion or a delivery when there is a hypervascular area with turbulent flow within the myometrium. The majority of vascular lesions in the uterus following abortion are due to retained products, for which curettage is the treatment of choice; if curettage is not performed for fear of heavy bleeding, many patients will undergo preventable blood loss. Some patients may also be exposed to unnecessary invasive procedures such as embolization or hysterectomy due to intractable bleeding.

Care needs to be taken before diagnosing AVMs during pregnancy and after abortion. All patients showing a hypervascular lesion in the myometrium must undergo work-up for retained product of the conceptus. Patients who have high levels of β-hCG and are hemodynamically stable can safely undergo curettage; follow-up should include monitoring hCG levels and Doppler ultrasound until complete regression of the vascular lesions is seen. Patients who are hemodynamically unstable can have angiography and embolization.

Gestational trophoblastic tumors are highly vascular and are associated with the formation of uterine vascular malformations. These vascular malformations persist in 10% to 15% of patients, even after complete resolution of the tumor following chemotherapy. Overall, 1% to 2% of these uterine vascular malformations cause vaginal or intraperitoneal hemorrhage, which can be life threatening.[58,59]

Gestational trophoblastic disease demonstrates increased vascularity with low-resistance arterial flow and low PI because the proliferation

of trophoblastic tissue and its invasion of the endometrium and myometrium lead to development of abundant small vessels that penetrate the invading trophoblast, coupled with a prominent arteriovenous shunt.[60]

Eradication of vascular malformations with embolization would therefore be expected to lead to normalization of uterine artery PI values.[61] However, low postembolization PI values would imply a persistent vascular malformation and, therefore, an increased risk for recurrent hemorrhage.

Once the correct diagnosis of a uterine AVM is made, further treatment is based on the clinical status of the patient. Patients who are anemic or hemodynamically unstable should be referred for angiography and embolization. Patients with a single episode of bleeding who are hemodynamically stable can be treated conservatively. Many of these patients will remain asymptomatic, suggesting that traumatic AVMs do spontaneously regress.[62]

Long-term medical management may be used if the bleeding is not severe and includes estrogens and progestins, methylergonovine, danazol, 15-methyl prostaglandin F2α, oral contraceptives, and intramuscular followed by oral methylergonovine maleate.[63] Recently, Montanari and Alfei[64] reported a patient with AVM who was treated with intravenous conjugated estrogens and oral methylergometrine maleate. The authors hypothesized that methylergometrine maleate induces tetanic myometrial contractions and reduces the blood flow to the AVM, making it collapse, and intravenous conjugated estrogens help by covering the hemorrhaging vessels with proliferative endometrium. There have also been reports of use of a gonadotropin-releasing hormone antagonist[65] and danazol[66] for treatment of AVMs.

Angiographic UAE is the preferred therapy for uterine AVMs, especially in young women who desire to preserve fertility because it does not appear to interfere with the menstrual cycle or pregnancy. Poppe and colleagues[67] documented normal placental flow by Doppler ultrasonography in a gravid patient who had previously undergone pelvic embolization. There are no reports of infertility or fetal growth restriction following embolization. O'Brien and associates[68] reported that normal menstrual cycle returned in 2 months in all 11 women following embolization, and 5 of them subsequently became pregnant.

Earlier reports described the use of an absorbable gelatin compressed sponge as the material of choice for embolization because the 3- to 5-week duration of occlusion is sufficient to prevent further hemorrhage while permitting slow development of collateral vessels and thus preventing ischemia.[69] More recent studies have suggested polyvinyl alcohol particles[70] or glue (n-butyl cyanoacrylate)[71] as agents of choice. Varying degrees of pelvic pain are common in the immediate postembolization period.[72] This is easily controlled with a patient-controlled analgesia pump. Serious complications, usually due to internal iliac artery embolization, the use of glue as the embolic agent, or both, are extremely rare. These complications include perianal skin sloughing, uterovaginal and rectovaginal fistulas, and neurologic deficits in the lower extremities.[73]

Other surgical managements reported less frequently are coagulation of the AVM under hysteroscopic guidance, surgical removal of an AVM, laparoscopic bipolar coagulation of uterine vessels,[74] and ligation of the uterine artery.[75] Currently, hysterectomy is indicated only for those women who do not need fertility preservation and have limited access to medical facilities.[76]

AVM Combined With a Pseudoaneurysm. D&C, cesarean delivery, or other trauma to the uterus may cause a pseudoaneurysm, an AVM, or both. The vessels of an AVM are apt to be injured even by minute trauma, with a resulting concomitant pseudoaneurysm.[77]

Absorbable gelatin sponge pledgets are usually the material of choice for embolization of acquired AVMs, pseudoaneurysms arising from small branches, cases of combined AVM and pseudoaneurysm, and direct arterial rupture because of the ease of delivery and the duration of effect. The 3- to 5-week duration of occlusion by absorbable gelatin sponge pledgets is sufficient to stop hemorrhage while still permitting slow development of collateral vessels.[32] For occlusion of the proximal vessel in cases of pseudoaneurysms arising from larger branches or large AVF, metallic coils are preferred because of the risk of shunting of particulate embolic materials via a fistula into the systemic circulation or into the pseudoaneurysm.

Conclusions

Vascular lesions of the uterus are more common than previously thought. Patients presenting with menorrhagia and delayed secondary hemorrhage following surgical intervention, pregnancy, or abortion have to be evaluated for possible AVMs. Color Doppler is the standard screening investigation, with 3D power color angiography emerging as a popular choice for diagnosing AVM. Patients diagnosed as having dangerous AVM need to undergo angiography to confirm diagnosis and then undergo UAE. Care must be taken

during diagnosis of postpregnancy or postabortion AVM and all patients must be evaluated for retained product of conceptus with carefully measured β-hCG levels. This can avoid subjecting patients to unnecessary invasive angiography and UAE. ■

References

1. Timmerman D, Wauters J, Van Calenbergh S, et al. Color Doppler imaging is a valuable tool for the diagnosis and management of uterine vascular malformations. *Ultrasound Obstet Gynecol*. 2003;21:570-577.
2. Rufener SL, Adusumilli S, Weadock WJ, Caoili E. Sonography of uterine abnormalities in postpartum and postabortion patients: a potential pitfall of interpretation. *J Ultrasound Med*. 2008;27:343-348.
3. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg*. 1982;69:412-422.
4. Nasu K, Nishida M, Yoshimatsu J, Narahara H. Ectopic pregnancy after successful treatment with percutaneous transcatheter uterine arterial embolization for congenital uterine arteriovenous malformation: a case report. *Arch Gynecol Obstet*. 2008;278:171-172.
5. O'Brien P, Neyastani A, Buckley AR, et al. Uterine arteriovenous malformations: from diagnosis to treatment. *J Ultrasound Med*. 2006;25:1387-1392.
6. Beller U, Rosen RJ, Beckman EM, et al. Congenital arteriovenous malformation of the female pelvis: a gynecological perspective. *Am J Obstet Gynecol*. 1988;159:1153-1160.
7. Kasznica J, Nisar N. Congenital vascular malformation of the uterus in a stillborn: a case report. *Hum Pathol*. 1995;26:240-241.
8. Geary M, McParland P. Multiple and massive arteriovenous malformations in pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 1996;64:147-150.
9. Weiss SW, Goldblum JR, Enzinger FM. *Enzinger and Weiss's Soft Tissue Tumors*. St Louis, MO: Mosby; 2001.
10. Johnson C, Reid-Nicholson M, Deligdisch L, et al. Capillary hemangioma of the endometrium: a case report and review of the literature. *Arch Pathol Lab Med*. 2005;129:1326-1329.
11. Djunic I, Elezovic I, Ljubic A, et al . Diffuse cavernous hemangioma of the left leg, vulva, uterus, and placenta of a pregnant woman. *Int J Gynaecol Obstet*. 2009;107:250-251.
12. Malhotra S, Sehgal A, Nijhawan R. Cavernous hemangioma of the uterus. *Int J Gynaecol Obstet*. 1995;51:159-160.
13. Virk RK, Zhong J, Lu D. Diffuse cavernous hemangioma of the uterus in a pregnant woman: report of a rare case and review of literature. *Arch Gynecol Obstet*. 2008;279:603-605.
14. Thanner F, Suetterlin M, Kenn W, et al. Pregnancy-associated diffuse cavernous hemangioma of the uterus. *Acta Obstet Gynecol Scand*. 2001;80:1150-1151.
15. Kuhnel P. Placental chorioangioma. *Acta Obstet Gynecol Scand*. 1933;13:143-145.
16. Marchetti AA. A consideration of certain types of benign tumors of the placenta. *Surg Gynecol Obstet*. 1939;68:733-743.
17. Sepulveda W, Aviles G, Car stens E, et al. Prenatal diagnosis of solid placental masses: the value of color flow imaging. *Ultrasound Obstet Gynecol*. 2000;16:554-558.
18. Zalel Y, Weisz B, Gamzu R, et al. Chorioangiomas of the placenta: sonographic and Doppler flow characteristics. *J Ultrasound Med*. 2002;21:909-913.
19. Quintero RA, Reich H, Romero R, et al. In utero endoscopic devascularization of a large chorioangioma. *Ultrasound Obstet Gynecol*. 1996;8:48-52.
20. Heo H, Chazotte C, Dayal A, Dar P. Successful ablation of complicated placental chorioangioma using ethyl alcohol as a sclerosant. *Ultrasound Obstet Gynecol*. 2009;34(suppl 1):251.
21. As AK, Hagen P, Webb JB, Wijesinghe D. Therapeutic amniodrainage in chorioangioma. *J Obstet Gynecol*. 1997;17:169-170.
22. Boon LM, Mulliken JB, Enjolras O, Vikkula M. Glomuvenous malformation (glomangioma) and venous malformation: distinct clinicopathologic and genetic entities. *Arch Dermatol*. 2004;140:971-976.
23. Burrows PE, Mason KP. Percutaneous treatment of low flow vascular malformations. *J Vasc Interv Radiol*. 2004;15:431-445.
24. Polat P, Suma S, Kantarcý M, et al. Color Doppler US in the evaluation of uterine vascular abnormalities. *Radiographics*. 2002;22:47-53.
25. Hsieh FJ, Wu CC, Lee CN, et al. Vascular patterns of gestational trophoblastic tumors by color Doppler ultrasound. *Cancer*. 1994;74:2361-2365.
26. Kazmier FJ, Harrison CE Jr. Acquired aortocaval fistulas. *Am J Med*. 1973;55:175-183.
27. Fulmer GT Jr, Mayberger HW, Sheehy TJ, Hayden CW. Arteriovenous fistula of the uterine artery. A rare complication of hysterectomy. *Angiology*. 1970;21:647-653.
28. Laurian C, Leclef Y, Gigou F, et al. Pelvic arteriovenous fistulas: therapeutic strategy in five cases. *Ann Vasc Surg*. 1990;4:1-9.
29. Morley GW, Lindenauer SM. Arteriovenous fistula following pelvic operations. *Obstet Gynecol*. 1968;31:722-726.
30. Wideman GL, Gravlee LC, Jones WN. Arteriovenous aneurysm of the uterine artery and vein following total abdominal hysterectomy; report of a case. *Am J Obstet Gynecol*. 1959;78:200-203.
31. Decker DG, Fish CR, Juergens JL. Arteriovenous fistulas of the female pelvis. A diagnostic problem. *Obstet Gynecol*. 1968;31:799-805.
32. Novak D. Embolization materials. In: Dondelinger RF, Rossi P, Kurdziel JC, Wallace S, eds. *Interventional Radiology*. New York, NY: Thieme; 1990: 295-313.
33. Cronin P, McPherson SJ, Meaney JF, Mavor A. Venous covered stent: successful occlusion of a symptomatic internal iliac arteriovenous fistula. *Cardiovasc Intervent Radiol*. 2002;25:323-325.
34. Higón MA, Domingo S, Bauset C, et al. Hemorrhage after myomectomy resulting from pseudoaneurysm of the uterine artery. *Fertil Steril*. 2007;87:417.e5-e8.

MAIN POINTS

- Vascular lesions of the uterus, either congenital or acquired, are very rare; most reported in the literature are arteriovenous malformations (AVMs). Many studies report spontaneous resolution of vascular lesions during follow-up; in addition, there is an increasing trend toward use of uterine artery embolization (UAE) as a method of treatment.
- Hemangiomas associated with pregnancy are best managed with vaginal delivery; it is important to remember that vascular lesions increase in size during pregnancy and are at risk of causing postpartum hemorrhage. Pseudoaneurysm of the uterine artery is an uncommon cause of delayed postpartum hemorrhage following cesarean or vaginal delivery and is potentially life threatening.
- Venous malformations are readily diagnosed by magnetic resonance imaging. It is important to correctly identify various vascular lesions in the uterus to avoid unnecessary invasive intervention. Three-dimensional color power angiography also allows the physician to examine vascular anatomy immediately and without radiation exposure or invasive angiogram.
- Angiographic UAE is the preferred therapy for uterine AVMs, especially in young women who desire to preserve fertility. Other surgical managements reported less frequently are coagulation of the AVM under hysteroscopic guidance, surgical removal of an AVM, laparoscopic bipolar coagulation of uterine vessels, and ligation of the uterine artery.

35. Matsubara S. Uterine artery pseudoaneurysm after cesarean section: case report and literature review. *J Minim Invasive Gynecol*. 2011;18:411-412.
36. Langer JE, Cope C. Ultrasonographic diagnosis of uterine artery pseudoaneurysm after hysterectomy. *J Ultrasound Med*. 1999;18:711-714.
37. Hennerici M, Neuerburg-Heusler D. Peripheral arteries. In: Hennerici M, Neuerburg-Heusler D, eds. *Vascular Diagnosis with Ultrasound*. New York, NY: Thieme, 1998;133-187.
38. Zimon AE, Hwang JK, Principe DL, Bahado-Singh RO. Pseudoaneurysm of the uterine artery. *Obstet Gynecol*. 1999;94:827-830.
39. Bromley PJ, Clark T, Weir IH, Zwirewich CV. Radiologic diagnosis and management of uterine artery pseudoaneurysm: case report. *Can Assoc Radiol J*. 1997;48:119-122.
40. Pelage JP, Le Dref OL, Mateo J, et al. Life-threatening primary postpartum hemorrhage: treatment with emergency selective arterial embolization. *Radiology*. 1998;208:359-362.
41. Pelage JP, Soyer P, Repiquet D, et al. Secondary postpartum hemorrhage: treatment with selective arterial embolization. *Radiology*. 1999;212:385-389.
42. Revencu N, Boon LM, Mulliken JB, et al. Parkes Weber syndrome, vein of Galen aneurysmal malformation, and other fast-flow vascular anomalies are caused by RASA1 mutations. *Hum Mutat*. 2008;29:959-965.
43. Takaya N, Iwase T, Maehara A, et al. Transcatheter embolization of arteriovenous malformations in Cowden disease. *Jpn Circ J*. 1999;63:326-329.
44. Dahlgren LS, Effer SB, McGillivray BC, Pugash DJ. Pregnancy with uterine vascular malformations associated with hemorrhagic hereditary telangiectasia: a case report. *J Obstet Gynaecol Can*. 2006;28:720-723.
45. Fleming H, Ostör AG, Pickel H, Fortune DW. Arteriovenous malformations of the uterus. *Obstet Gynecol*. 1989;73:209-214.
46. Roven SJ. Arteriographic evaluation of vascular malformations. In: Kim D, Orron DE, eds. *Peripheral Vascular Imaging and Intervention*. St Louis, Mo: Mosby; 1991;165-170.
47. Follen MM, Fox HE, Levine RU. Cervical vascular malformation as a cause of antepartum and intrapartum bleeding in three diethylstilbestrol-exposed progeny. *Am J Obstet Gynecol*. 1985;153:890-891.
48. Manolitsas T, Hurley V, Gilford E. Uterine arteriovenous malformation—a rare cause of uterine haemorrhage. *Aust N Z J Obstet Gynaecol*. 1994;34: 197-199.
49. Uchide K, Suzuki N, Murakami K, et al. Uterine arteriovenous malformation as a cause of immediate postpartum hemorrhage. *Acta Obstet Gynecol Scand*. 1998;77:577-580.
50. Shih JC, Shyu MK, Cheng WF, et al. Arteriovenous malformation of mesosalpinx associated with a 'vanishing' ectopic pregnancy: diagnosis with three-dimensional color power angiography. *Ultrasound Obstet Gynecol*. 1999;13:63-66.
51. Valsky DV, Hamani Y, Verstandig A, Yagel S. The use of 3D rendering, VCI-C, 3D power Doppler and B-flow in the evaluation of interstitial pregnancy with arteriovenous malformation treated by selective uterine artery embolization. *Ultrasound Obstet Gynecol*. 2007;29:352-355.
52. Cohen JM, Weinreb JC, Redman HC. Arteriovenous malformations of the extremities: MR imaging. *Radiology*. 1986;158:475-479.
53. Vogelzang RL, Nemcek AA Jr, Skrtic Z, et al.Uterine arteriovenous malformations: primary treatment with therapeutic embolization. *J Vasc Intervent Radiol*. 1991;2:517-522.
54. Laing FC, Frates MC. Ultrasound evaluation during the first trimester of pregnancy. In: Callen PW, ed. *Ultrasonography in Obstetrics and Gynecology*. Philadelphia, PA: WB Saunders; 2000;127-128.
55. Dillon EH, Case CQ, Ramos IM, et al. Endovaginal US and Doppler findings after first-trimester abortion. *Radiology*. 1993;186:87-91.
56. Kido A, Togashi K, Koyama T, et al. Retained products of conception masquerading as acquired arteriovenous malformation. *J Comput Assist Tomogr*. 2003;27:88-92.
57. Wiebe ER, Switzer P. Arteriovenous malformations of the uterus associated with medical abortion. *Int J Obstet Gynecol*. 2000;71:155-158.
58. Newlands ES, Bagshawe KD, Begent RHJ, et al. Developments in chemotherapy for medium- and high-risk patients with gestational trophoblastic tumours (1979-1984). *Br J Obstet Gynaecol*. 1986;93:63-69.
59. McIvor J, Cameron EW. Pregnancy after uterine embolization to control haemorrhage from gestational trophoblastic tumours. *Br J Radiol*. 1996;69: 624-629.
60. Long MG, Boultbee JE, Langley R, et al. Doppler assessment of the uterine circulation and the clinical behaviour of gestational trophoblastic tumours requiring chemotherapy. *Br J Cancer*. 1992;66:883-887.
61. McGrath S, Harding V, Lim AK, et al. Embolization of uterine arteriovenous malformations in patients with gestational trophoblastic tumors: a review of patients at Charing Cross Hospital, 2000-2009. *J Reprod Med*. 2012;57:319-324.
62. Dar P, Karmin I, Einstein MH. Arteriovenous malformations of the uterus: long-term follow-up. *Gynecol Obstet Invest*. 2008;66:157-161.
63. Elia G, Counsell C, Singer SJ. Uterine artery malformation as a hidden cause of severe uterine bleeding; a case report. *J Reprod Med*. 2001;46:398-400.
64. Montanari L, Alfei A. Arteriovenous malformation of the uterus: successful pregnancy after medical treatment. *Ultrasound Obstet Gynecol*. 2007; 30:585.
65. Morikawa M, Yamada T, Yamada H, Minakami H. Effect of gonadotropin-releasing hormone agonist on a uterine arteriovenous malformation. *Obstet Gynecol*. 2006;108(3 Pt 2):751-753.
66. Takeuchi K, Yamada T, Iwasa M, Maruo T. Successful medical treatment with danazol after failed embolization of uterine arteriovenous malformation. *Obstet Gynecol*. 2003;102:843-844.
67. Poppe W, Assche FA, Wilms G, et al. Pregnancy after transcatheter embolization of a uterine arteriovenous malformation. *Am J Obstet Gynecol*. 1987;156: 1179-1180.
68. O'Brien P, Neyastani A, Buckley AR, et al. Uterine arteriovenous malformations from diagnosis to treatment. *J Ultrasound Med*. 2006;25:1387-1392.
69. Vedantham S, Goodwin SC, McLucas B, Mohn G. Uterine artery embolization: an underused method of controlling pelvic hemorrhage. *Am J Obstet Gynecol*. 1997;176:938-948.
70. Lim AK, Agarwal R, Seckl MJ, et al. Embolization of bleeding residual vascular malformations in patients with treated gestational trophoblastic tumours. *Radiology*. 2002;222:640-644.
71. Ghai S, Rajan DK, Asch MR, et al. Efficacy of embolization in traumatic uterine vascular malformations. *J Vasc Interv Radiol*. 2003;14:1401-1408.
72. Greenwood LH, Glickman MG, Schwartz PE, et al. Obstetric and non-malignant gynecological bleeding: treatment with angiographic embolization. *Radiology*. 1987;164:155-159.
73. Hare WS, Holland CJ. Paresis following internal iliac artery embolization. *Radiology*. 1983;146:47-51.
74. Corusic A, Barisic D, Lovric H, et al. Successful laparoscopic bipolar coagulation of a large arteriovenous malformation due to invasive trophoblastic disease: a case report. *J Minim Invasive Gynecol*. 2009;16:368-371.
75. Yokomine D, Yoshinaga M, Baba Y, et al. Successful management of uterine arteriovenous malformation by ligation of feeding artery after unsuccessful uterine artery embolization. *J Obstet Gynaecol Res*. 2009;35:183-188.
76. Bagga R, Verma P, Aggarwal N, et al. Failed angiographic embolization in uterine arteriovenous malformation: a case report and review of the literature. *Medscape J Med*. 2008;10:12.
77. Roche A. Peripheral arteriovenous malformations. In: Dondelinger RF, Rossi P, Kurdziel JC, Wallace S, eds. *Interventional Radiology*. New York, NY: Thieme; 1990:518-528.